

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/19544

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61K 39/395; C07K 16/00  
US CL : 424/133.1, 135.1, 181.1, 183.1; 530/387.3, 387.7

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
U.S. : 424/133.1, 135.1, 181.1, 183.1; 530/387.3, 387.7

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
Please See Continuation Sheet

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	ST. CROIX, B. et al. Genes expressed in human tumor endothelium. Science. 18 August 2000, Vol. 289, pages 1197-1202, see entire document.	1-9
X	LORENZ, A. et al. Evidence for direct physical association between a K <sup>+</sup> channel (Kir6.2) and an ATP-binding cassette protein (SUR1) which affects cellular distribution and kinetic behavior of an ATP-sensitive K <sup>+</sup> channel. Molecular & Cellular Biology. March 1998, Vol. 18, No. 3, pages 1652-1659, see entire document.	1
Y	US 6,559,128 B1 (HAMM et al) 06 May 2003(06.05.2003), column 1 lines 40-45, column 4 lines 48-65, column 10 lines 60-67.	2-9
Y	ELEANOR, B. et al. Cell surface tumor endothelial markers are conserved in mice and humans. Cancer Research. 15 September 2001, Vol. 61, pages 6649-6655, see entire document.	1-9

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

\* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance  
"E" earlier application or patent published on or after the international filing date  
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)  
"O" document referring to an oral disclosure, use, exhibition or other means  
"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention  
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone  
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art  
"&" document member of the same patent family

Date of the actual completion of the international search

04 November 2003 (04.11.2003)

Date of mailing of the international search report

22 DEC 2003

Name and mailing address of the ISA/US

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## Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claim Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claim Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:  
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-9 (potassium inwardly-rectifying channel)

Remark on Protest

☐  
☐

- The additional search fees were accompanied by the applicant's protest.  
No protest accompanied the payment of additional search fees.

**BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING**

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

- I. Claims 1-9, drawn to an antibody that binds an extracellular domain of a TEM protein.
- II. Claims 10-15, drawn to a method of inhibiting neoangiogenesis with an antibody.
- III. Claim 16, drawn to a method of inhibiting tumor growth with an antibody.
- IV. Claims 17-20, drawn to a method of identifying a ligand involved in endothelial cell regulation using a human transmembrane protein.
- V. Claims 21-24, drawn to a method of identifying a ligand involved in endothelial cell regulation using a test compound and an antibody.
- VI. Claims 25-27, drawn to a method of identifying a ligand involved in endothelial cell regulation using a test compound and a human transmembrane protein.
- VII. Claims 28-29, drawn to a soluble form of a human transmembrane protein.
- VIII. Claims 30-35, drawn to a method of inhibiting neoangiogenesis using a human transmembrane protein.
- IX. Claim 36, drawn to a method of identifying regions of neoangiogenesis using an antibody.
- X. Claim 37, drawn to a method of screening for neoangiogenesis using an antibody.
- XI. Claims 38-47, drawn to a method of identifying candidate drugs for treating tumors or wounds.
- XII. Claims 48-51, drawn to a method of identifying endothelial cells.
- XIII. Claims 52-53, drawn to a method of inducing an immune response.
- XIV. Claim 54, drawn to a method of stimulating vascular proliferation.

Groups I-XIV as set forth above are drawn to a plurality of 71 distinct TEM molecules. Therefore, for each of groups I-XIV there are 71 different groups or a total of 994 inventions.

The inventions listed as Groups I-XIV do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The technical feature linking groups I-XIV appears to be that they all relate to a human transmembrane protein and antibodies that bind the extracellular domain of a human transmembrane protein.

However, YAUCH R. L. et al. (The Journal of Biological Chemistry. Direct extracellular contact between integrin alpha-3-beta-1 and TM4SF protein CD151. 13 March 2000. Vol. 275, No. 13, pages 9230-9238.) teaches a monoclonal antibody that binds to the extracellular domain of CD151.

Therefore, the technical feature linking the inventions of groups I-V does not constitute a special technical feature as defined by PCT rule 13.2, as it does not define a contribution over the prior art.

The special technical feature of Group I is considered to be an antibody that binds an extracellular domain of a TEM protein.

The special technical feature of group II is considered to be an antibody that binds an extracellular domain of a TEM protein.

The special technical feature of group III is considered to be an antibody that binds an extracellular domain of a TEM protein.

The special technical feature of group IV is considered to be a human transmembrane protein.

The special technical feature of group V is considered to be an antibody that binds an extracellular domain of a TEM protein.

The special technical feature of group VI is considered to be a human transmembrane protein.

The special technical feature of group VII is considered to be a human transmembrane protein.

The special technical feature of group VIII is considered to be a human transmembrane protein.

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The special technical feature of group IX is considered to be an antibody that binds an extracellular domain of a TEM protein.

The special technical feature of group X is considered to be an antibody that binds an extracellular domain of a TEM protein.

The special technical feature of group XI is considered to be a human transmembrane protein.

The special technical feature of group XII is considered to be an antibody that binds an extracellular domain of a TEM protein.

The special technical feature of group XIII is considered to be a human transmembrane protein.

The special technical feature of group XIV is considered to be a human transmembrane protein.

Accordingly, Groups I-XIV are not so linked by the same or a corresponding special technical feature as to form a single general inventive concept.

### Continuation of B. FIELDS SEARCHED Item 3:

MEDLINE, BIOSIS, WEST

Search terms: TEM, Kir, GIRK, rectifying inwardly K<sup>+</sup> channel, antibody, inventor name search.